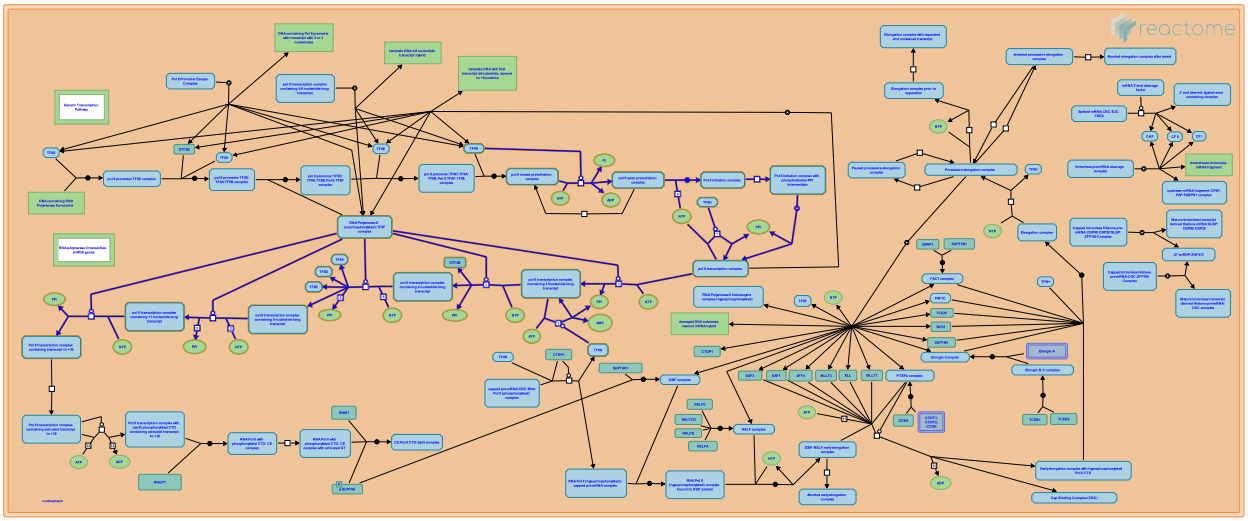
# RNA Polymerase II Transcription Initiation And Promoter Clearance



Joshi-Tope, G., Timmers, HTM.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.



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# Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.
The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

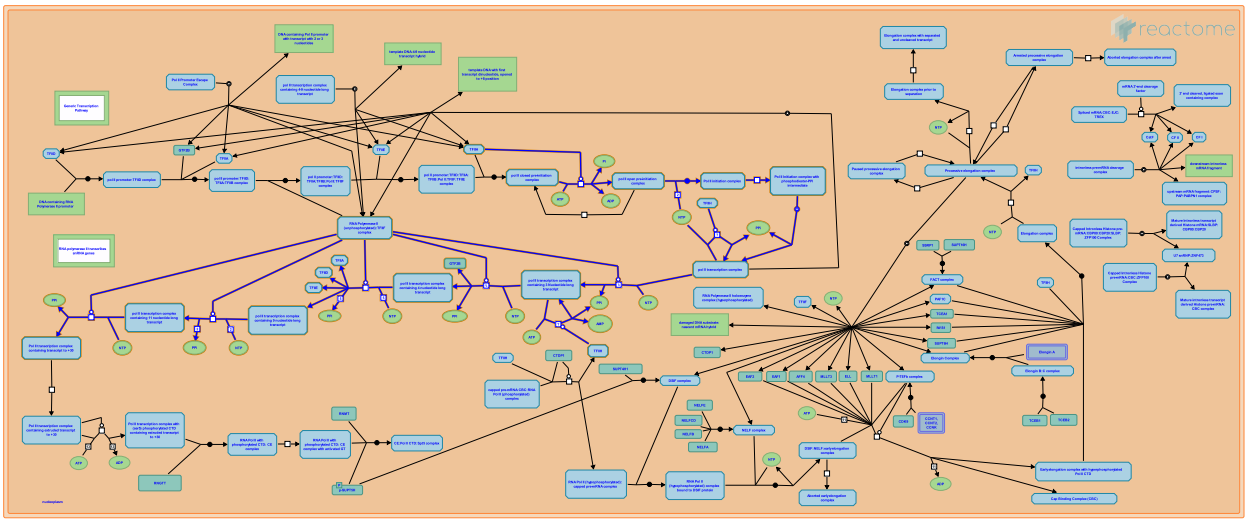
Reactome database release: 88

This document contains 3 pathways and 1 reaction (see Table of Contents)

## RNA Polymerase II Transcription Initiation And Promoter Clearance ↗

**Stable identifier:** R-HSA-76042

**Compartments:** nucleoplasm



The transcription cycle is divided in three major phases: initiation, elongation, and termination. Transcription initiation include promoter DNA binding, DNA melting, and initial synthesis of short RNA transcripts. Many changes must occur to the RNA polymerase II (pol II) transcription complex as it makes the transition from initiation into transcript elongation. During this intermediate phase of transcription, contact with initiation factors is lost and stable association with the nascent transcript is established. These changes collectively comprise promoter clearance.

## Literature references

Luse, DS. (2013). Promoter clearance by RNA polymerase II. *Biochim. Biophys. Acta, 1829*, 63-8. ↗

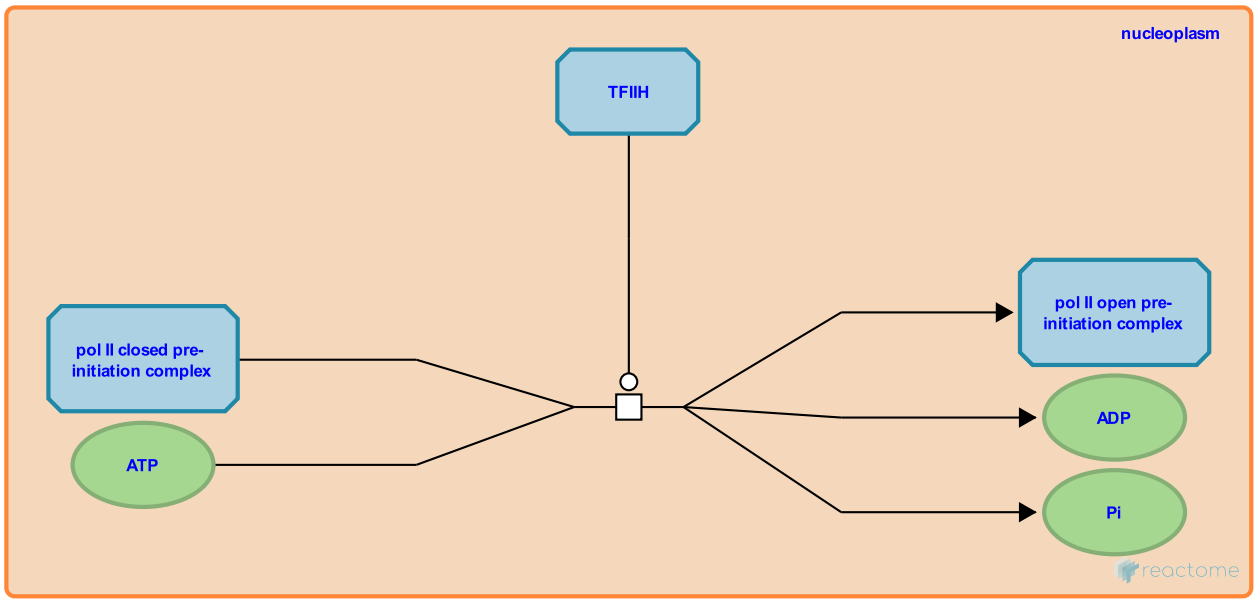
## RNA Polymerase II Promoter Opening: First Transition ↗

**Location:** RNA Polymerase II Transcription Initiation And Promoter Clearance

**Stable identifier:** R-HSA-75949

**Type:** transition

**Compartments:** nucleoplasm




After assembly of the complete RNA polymerase II-preinitiation complex, the next step is separation of the two DNA strands. This isomerization step is known as the closed-to-open complex transition and occurs prior to the initiation of mRNA synthesis. In the RNA polymerase II system this step requires the hydrolysis of ATP or dATP into Pi and ADP or dADP (in contrast to the other RNA polymerase systems) and is catalyzed by the XPB subunit of TFIIH. The region of the promoter, which becomes single-stranded , spans from –10 to +2 relative to the transcription start site.

Negative supercoiling in the promoter region probably induces transient opening events and can alleviate requirement of TFIIE, TFIIH and ATP-hydrolysis for open complex formation. ATP is also used in this step by the cdk7-subunit of TFIIH to phosphorylate the heptad repeats of the C-terminal domain of the largest subunit of RNA polymerase II (RPB1) on serine-2

## Literature references


Coin, F., Egly, JM., Tirode, F., Busso, D. (1999). Reconstitution of the transcription factor TFIIH: assignment of functions for the three enzymatic subunits, XPB, XPD, and cdk7. *Mol Cell, 3*, 87-95. ↗

Bunick, D., Zandomeni, R., Ackerman, S., Weinmann, R. (1983). Mechanism of RNA polymerase II--specific initiation of transcription in vitro: ATP requirement and uncapped runoff transcripts. *Cell, 29*, 877-86. ↗

Sharp, PA., Parvin, JD. (1993). DNA topology and a minimal set of basal factors for transcription by RNA polymerase II. *Cell, 73*, 533-40. ↗

Fiedler, U., Marc Timmers, HT. (2000). Peeling by binding or twisting by cranking: models for promoter opening and transcription initiation by RNA polymerase II. *Bioessays, 22*, 316-26. ↗

Goodrich, JA., Tjian, R. (1994). Transcription factors IIE and IIH and ATP hydrolysis direct promoter clearance by RNA polymerase II. *Cell, 77*, 145-56. ↗


## Editions

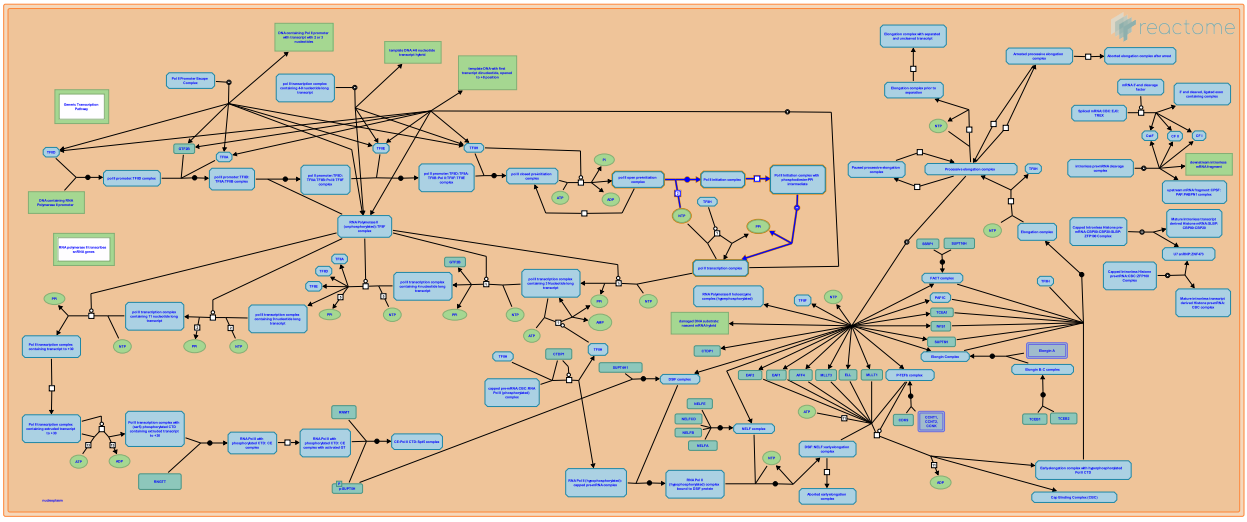
| | | |
|---|---|---|
| 2003-09-11 | Authored | Timmers, HTM. |
| 2024-03-06 | Edited | Joshi-Tope, G. |

## RNA Polymerase II Transcription Initiation ↗

**Location:** RNA Polymerase II Transcription Initiation And Promoter Clearance

**Stable identifier:** R-HSA-75953

**Compartments:** nucleoplasm



Formation of the open complex exposes the template strand to the catalytic center of the RNA polymerase II enzyme. This facilitates formation of the first phosphodiester bond, which marks transcription initiation. As a result of this, the TFIIB basal transcription factor dissociates from the initiation complex.

The open transcription initiation complex is unstable and can revert to the closed state. Initiation at this stage requires continued (d)ATP-hydrolysis by TFIIH. Dinucleotide transcripts are not stably associated with the transcription complex. Upon dissociation they form abortive products. The transcription complex is also sensitive to inhibition by small oligo-nucleotides.

Dinucleotides complementary to position -1 and +1 in the template can also direct first phosphodiester bond formation. This reaction is independent on the basal transcription factors TFIIE and TFIIH and does not involve open complex formation. This reaction is sensitive to inhibition by single-stranded oligonucleotides.

## Literature references


Goodrich, JA., Kugel, JF. (2002). Translocation after synthesis of a four-nucleotide RNA commits RNA polymerase II to promoter escape. *Mol Cell Biol, 22*, 762-73. ↗

Jacob, GA., Luse, DS. (1987). Abortive initiation by RNA polymerase II in vitro at the adenovirus 2 major late promoter. *J Biol Chem, 262*, 14990-7. ↗

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van der Vliet, PC., Timmers, HT., Holstege, FC. (1996). Opening of an RNA polymerase II promoter occurs in two distinct steps and requires the basal transcription factors IIE and IIH. *EMBO J, 15*, 1666-77. ↗


## Editions

| | | |
|---|---|---|
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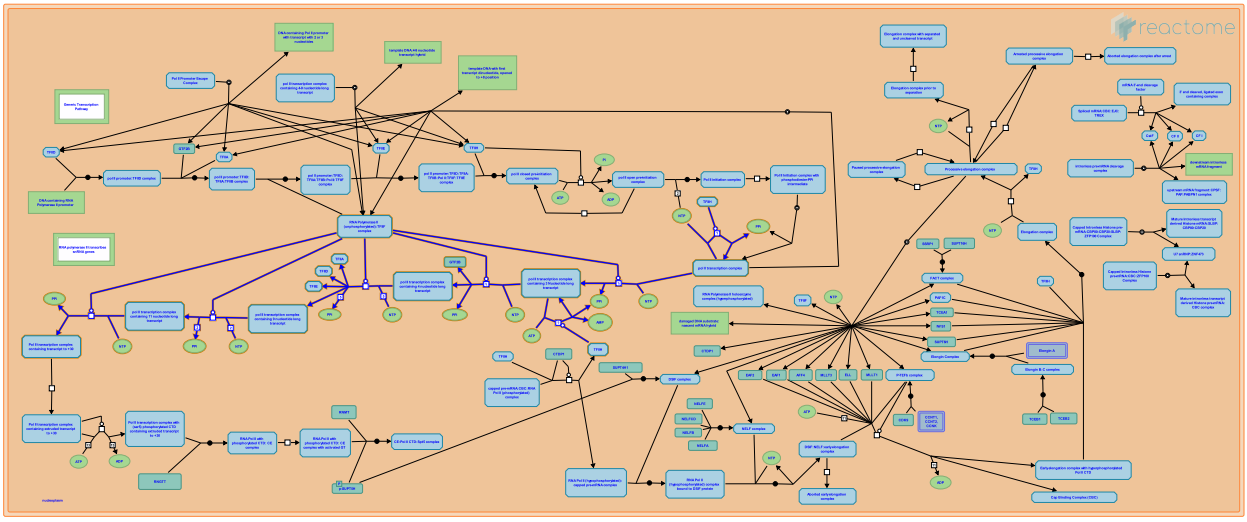
| 2024-03-06 | Edited | Joshi-Tope, G. |

## RNA Polymerase II Promoter Escape ↗

**Location:** RNA Polymerase II Transcription Initiation And Promoter Clearance

**Stable identifier:** R-HSA-73776

**Compartments:** nucleoplasm



RNA Polymerase II promoter escape occurs after the first phosphodiester bond has been created.

## Literature references


Fiedler, U., Timmers, HT., Holstege, FC. (1998). Three transitions in the RNA polymerase II transcription complex during initiation. *EMBO J, 16*, 7468-80. ↗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